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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,966	03/22/2002	Reiner Grabowski	216180	4911

23460 7590 11/15/2006

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EXAMINER	
CALAMITA, HEATHER	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 11/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,966	GRABOWSKI ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *86,88,89,92-94,97,100,105 and 107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *86,88,89,92-94,97,100,105 and 107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. Amendments of August 24, 2006, have been received and entered in full. Claims 86, 88, 89, 92-94, 97, 100, 105 and 107 are pending and under examination. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 112

Claim Rejections - 35 USC § 112 (New Matter)

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 86, 88, 89, 92-94, 97, 100, 105 and 107 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 86, 88, 89, 92-94, 97, 100, 105 and 107 recite, "any species of the taxonomic unit of Enterobacteriaceae and no species of another taxonomic unit." Applicants assert support for this recitation appears in the specification at p. 10 lines 19-23 where the specification states "The synthesized PCR products are mostly of sizes on the order of 400 to 750 base pairs. Many bands can occur throughout, because ribosomal alleles are heterogeneous in many bacterial species. Table 1 shows the results obtained. They show that the enterobacteria are completely delimited from representatives of other taxa. While there is support for in the specification for detection of species of Enterobacteriaceae there is not support for the exclusion of other species and taxa. Applicants also point to the specification

at p. 25 lines 30-34, p. 27 lines 15-22 and p. 35 lines 9-24. Again there is no recitation present within these passages sufficient to support the requirement in the claims of "no species of another taxonomic unit." Therefore this recitation is not sufficient for support of the newly added limitation.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 86, 88, 89, 92-94, 97, 100, 105 and 107 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)
The current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The genus includes variants for which no written description is provided in the specification. Applicant has express description for SEQ ID NOs: 2 and 78 not the hundreds of nucleic acid sequences that are complements of SEQ ID NOs: 2 and 78. Thus, applicant has express possession of only 2 specific nucleic acids, namely SEQ ID NOs: 2 and 78, in a genus which comprises hundreds of thousands of different possibilities. Here, no common element or attributes of the sequences are

disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, complements of SEQ ID NOs: 2 and 78 is precisely the situation of naming a type of material which is generally known to likely exist, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a nucleotide sequence, without any definition of the particular changes due to selectively hybridizing language claimed.

In the instant application, certain specific no specific sequences are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids with a particular sequence. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 86, 88, 89, 92-94, 97 and 107 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mariani et al. (USPN 5,654,141, 08/05/1997) in view of Yamamoto et al. (Genebank Accession number AB001341, submitted January 25, 1997).

With regard to claim 86, Mariani et al. teach a method for detecting an enterobacteria in an analytical sample, comprising

the step of bringing the analytical sample into contact with an added nucleic acid or a combination of added nucleic acids, and detecting suitable hybrid nucleic acids comprising at least one of the added nucleic acids and bacterial nucleic acids wherein the one or more added nucleic acid is SEQ ID NO:2 (see col. 2 lines 10-16, and see col. 2 lines 52 and 54 and example 1, where *E. coli* are enterobacteria).

wherein any species of the taxonomic unit of Enterobacteriaceae but no species of another taxonomic unit is detected by formation of the hybrid nucleic acid (see col. 2 lines 10-16, and see col. 2 lines 52 and 54 and example 1, where *E. coli* are enterobacteria. Optionally, in a further step, the DNA fragments obtained by amplification which are specific for genera or species are detected by means of probes, wherein the primers used comprise SEQ ID NO: 2 see col. 8 lines 39-56. When detecting E. coli, Mariani detects only Enterobacteriaeceae and not species of another taxonomic unit).

With regard to claims 88 and 93, Mariani et al. teach the process involves a PCR amplification of the nucleic acid to be detected (see col. 5 lines 40-44).

With regard to claims 89 and 94, Mariani et al. teach in that the process involves a Southern Blot hybridization (see col. 8 lines 8-9).

With regard to claims 92, Mariani et al. teach a method for amplifying bacterial DNA of any species of the taxonomic unit of Enterobacteriaceae, using conserved primers (see col. 4 lines 21-29, and 38-43, where the 16S rRNA gene is conserved, and the target nucleic acids are from the class of Escherichia. Optionally, in a further step, the DNA fragments obtained by amplification which are specific for genera or species are detected by means of probes, wherein the primers used comprise SEQ ID NO: 2 (see col. 8 lines 39-56).

wherein any species of the taxonomic unit of Enterobacteriaceae but no species of another taxonomic unit is detected by formation of the hybrid nucleic acid (see col. 2 lines 10-16, and see col. 2 lines 52 and 54 and example 1, where *E. coli* are enterobacteria. Optionally, in a further step, the DNA fragments obtained by amplification which are specific for genera or species are detected by means of probes, wherein the primers used comprise SEQ ID NO: 2 see col. 8 lines 39-56. When detecting E. coli, Mariani detects only Enterobacteriaeceae and not species of another taxonomic unit).

With regard to claim 97, Mariani et al. teach the one or more added nucleic acid molecule or molecules is modified or labeled so that is can generate a signal in analytical detection procedures, with the modification being fluorescent (see col. 8 lines 1-20).

With regard to claim 107, Mariani et al. teach the modified or labeled groups are substances with affinity to enzymes or enzyme complexes (see col. 6 lines 53-54, where biotin is a substance with affinity to enzymes or enzyme complexes).

With regard to claims 86, 88, 89, 92-94, 97 and 107, Mariani et al. do not teach SEQ ID NO 2.

Yamamoto et al. teach SEQ ID NO 2, nucleic acid molecules complementary to SEQ ID NO: 2 and sequences with 90% identity to SEQ ID NO:2 (see alignment below).

Claimed SEQ ID NO: 2 1 ttcgggttgtcatgccaatg 20

Yamamoto et al. 11799 ttcgggttgtcatgccaatg 11780

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of Mariani with the use of functionally equivalent nucleic acid selected from the sequence of Yamamoto since Mariani expressly teaches primer selection using primers which amplify specific sequences in E. coli in order to detect the presence of the bacteria in patient samples.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers for the detection of E. coli and concerning

which a microbiologist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Response to Arguments

5. Applicants' arguments filed August 14, 2006, have been fully considered but they are not persuasive.

With respect to the 112 first paragraph written description rejections, regarding the recitation of 90% identity, Applicants arguments are persuasive. With respect to the written description rejection, regarding the recitation of "molecules complementary to" Applicants' arguments fail to address this issue, therefore the rejections are maintained.

With respect to the 103 (a) rejections, Applicants' argue "the claims have been amended to recite that the nucleic acid molecules consist of at least one or a combination of SEQ ID NO: 2 and SEQ ID NO:78" and that this amendment makes the rejection moot. This is not persuasive because the amendment does not require the sequence to consist of SEQ ID NO: 2 the claim requires the Markush group to consist of SEQ ID NO: 2 or SEQ ID NO: 78.

Applicants additionally argue, the Mariani patent does not teach the preamble of the instant claims, because the preamble recites a method of detecting any species of the taxonomic unit of enterobacteria and no other taxonomic unit. The Mariani patent teaches a method of detecting species other than those in the taxonomic unit of enterobacteria. This argument is not persuasive because the preamble does not limit the claim. The preamble serves only to recite an intended use for the method therefore it is not considered to give "life, meaning and vitality" to the claim. The claim preamble must be read in the context of the entire claim. The determination of whether preamble recitations are structural limitations or mere statements of purpose or use "can be resolved only on review of the entirety of the [record] to gain an understanding of what the inventors actually invented and intended to encompass by the claim." Corning Glass Works, 868 F.2d at 1257, 9 USPQ2d at 1966. If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction. Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999). See also Rowe v. Dror, 112 F.3d 473, 478, 42 USPQ2d 1550, 1553 (Fed. Cir. 1997) ("where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation"); Kropa v. Robie, 187 F.2d at 152, 88 USPQ2d at 480-81 (preamble is not a limitation where claim is directed to a product and the preamble merely recites a property inherent in an old product

defined by the remainder of the claim); STX LLC. v. Brine, 211 F.3d 588, 591, 54 USPQ2d 1347, 1350 (Fed. Cir.2000) (holding that the preamble phrase "which provides improved playing and handling characteristics" in a claim drawn to a head for a lacrosse stick was not a claim limitation). See MPEP 2111.02 for discussion on the determination of weight given to the preamble.

Allowable Subject Matter

6. The following is a statement of reasons for the indication of allowable subject matter: SEQ ID NO: 78 is free of the prior art.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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